SUMMARY OF SAFETY AND EFFECTIVENESS

I. GENERAL INFORMATION

Generic Name: A blood specimen collection and transportation device intended for home-use to obtain a dried blood spot (DBS) to be tested for antibodies to hepatitis C virus at a laboratory site.

Trade Name: Home Access® Hepatitis C Check℠ and Hepatitis C Check℠ Express

Applicant's Name and Address:
Home Access Health Corporation
2401 West Hassell Road, Suite 1510
Hoffman Estates, IL 60195-5200

Premarket Approval Application (PMA) Number: P980046

Date of Panel Recommendation: Pursuant to section 515 (c) of the act as amended by the safe Medical Devices Act of 1990, this PMA was not the subject of an FDA Microbiology Devices Advisory Panel meeting because the information in the PMA substantially duplicates information previously reviewed by the panel.

Date of Notice of Approval to the Applicant: April 28, 1999

II. INDICATIONS FOR USE

The Home Access Health Corporation Hepatitis C Check℠ and Hepatitis C Check℠ Express specimen collection and transport system is intended for home use for collection of a dried blood spot specimen by finger-stick, and is indicated for anonymous testing for antibody to hepatitis C virus (HCV) in adults, eighteen years or older, who may have been exposed to HCV through transfusion or organ transplant before 1992, who may have injected non-prescription drugs, or who were exposed to infected needles or had sexual contacts with HCV infected individuals.

Background

Currently there are two types of devices commercially available to test for the presence of antibodies to HCV: enzyme immunoassays (EIA), and a recombinant immunoblot supplemental assay (RIBA). These assays are only licensed for testing

serum and/or plasma specimens. While methods for analysis of dried blood spot specimens using both anti-HCV EIA and RIBA 3.0 have been demonstrated[1], applications for self-collected dried blood spot specimens to the tests listed above have not previously been published. However, there is literature to support the use of collection, elution, and testing dried blood spots for HIV[2,3,4].

Home Access® Hepatitis C Check℠ and Hepatitis C Check℠ Express were developed for self-collection of dried blood spots from finger-stick. The device is used at home to aid in detecting HCV antibodies in previously undiagnosed individuals. Home Access Health Corporation counselors provide support services to infected clients, inform them of professional health care providers in their locality if desired, and encourage them to notify sexual or needle-sharing partners.

III. DEVICE DESCRIPTION

The Home Access® Hepatitis C Check℠ and Hepatitis C Check℠ Express, (hereinafter referred to as Home Access® HCV Check℠) kit contains all the information and components required to use the device, and to collect and ship the specimen to a certified laboratory for testing, by U.S. Postal Service or Federal Express®.

The device consists of five product components used to support anonymous and confidential testing, and educational and counseling telemedicine service:

1) Home Access® HCV Check℠ Home Specimen Collection Kit. The device box includes (a) a blood collection card made of filter paper, imprinted with a unique Personal Identification Number (PIN); (b) two Safe-l-et lancets, alcohol prep swab, bandage and gauze pad for collection of the consumer's blood spot specimen; (c) a directional insert for use of the entire service containing an informed consent; (d) an HCV "Frequently Asked Questions" information booklet co-produced by the American Liver Foundation; and (e) materials for safe specimen shipment to a designated clinical laboratory. The device will be distributed as the Home Access® Hepatitis C Check℠ and Hepatitis C Check℠ Express. The only difference is the Home Access® HCV Check℠ contains a U.S. Postal Service envelope, and the HCV Check℠ Express contains a Federal Express® mailer.

2) Specimen Transport - U.S. Mail or commercial air express shipment of device specimens to a dedicated, certified clinical laboratory. The two modes of transport represent the only functional difference between the two product brand names:

Brand Name	Transport	Time-to-Result
HCV Check℠	U.S. Postal Service	10 Business Days
HCV Check℠ Express	Federal Express®	6 Business Days

Depending on the desired time to availability of results, the consumer will place the Blood Collection Card in the particular transport container system included in the kit selected for shipment of the specimens to the lab. The shippers included in both product embodiments contain both an inner envelope (Express only), a foil barrier pouch containing a desiccant, and an outer pre-paid, pre-printed, pre-addressed shipping envelope specific to the mode of transport.

3) Laboratory Procedures for anti-HCV Antibody Testing. A Clinical Laboratory Improvement Act (CLIA)-certified clinical laboratory dedicated to the Home Access Health Corporation (hereinafter referred to as Home Access) telemedicine service provides screening and supplemental testing for antibodies to HCV. All samples are shipped directly to, and tested at Mid-American Technologies, Olathe, KS, using an FDA licensed enzyme immunoassay and a recombinant immunoblot assay. The samples are tested according to the manufacturers' instructions for the device and proprietary dried blood spot elution and testing procedures.

4) Interactive Voice-Response (IVR) System, Automated Educational Risk Reduction Announcements, and Client Information Management and Results Retrieval. The clients' electronic access to the telemedicine service is available primarily by touch-tone telephone and e-mail. It allows the user to (a) activate the unique device registration and results retrieval PIN number; (b) obtain important pretest HCV risk reduction educational information; (c) record user responses to HCV demographic risk inquiries which improves the effectiveness of the service; and (d) retrieve negative results in an automated manner. These components support, respectively, (a) digital tone modulated frequency (DTMF) (i.e. touch-tone phone) activation of the unique device registration and results retrieval number; (b) automated recordings containing pretest HCV risk reduction information; (c) consumer entry of consumer responses to HCV demographic risk inquiries; and (d) DTMF retrieval of negative results.

5) Counseling and Referral Services. Home Access maintains a staff of certified healthcare counselors at its facility in Hoffman Estates, IL, that is available online 24 hours/day 7 days/week to respond to consumer HCV questions and concerns. Counseling services also provide referrals at the consumer's request to clinics and physicians skilled in HCV treatment. While most clients may access the majority of the telemedicine services using the automated systems, every user has the option to speak to a trained and certified healthcare counselor at any time during the testing process.

All test results are released by the laboratory Medical Director to Home Access for personal notification to the consumer (only negative results may be automatically accessed via the IVR system). The test results are anonymous and confidential, however, the consumer can direct Home Access to release the test results to a third party health care provider of his/her choice. All test results are available for 6 months after the test result is released to Home Access. However, counseling services are available at any time to all consumers possessing a valid Home Access Code Number. Counselors provide referrals for infected individuals to clinics, physicians, and/or psychosocial counselors, based upon their geographic proximity to the kit user (as determined by the ZIP code entered during pre-test demographic inquiry). Health care providers are pre-qualified by the counseling staff under the direction of the Medical Director for their expertise in HCV management and treatment prior to being provided as a referral.

IV. CONTRAINDICATIONS, WARNING AND PRECAUTIONS

There are no known contraindications for use of the Home Access® HCV Check℠.

For warnings and precautions refer to the package insert.

V. ALTERNATIVE PRACTICES AND PROCEDURES

The only tests currently licensed by the FDA for diagnosis of HCV infection are those that detect antibody to HCV. Two types of analytical systems are available: enzyme immunoassays (EIAs) used primarily for diagnosis of persons at risk for the disease as well as for the screening of blood donors, and a recombinant immunoblot assay (RIBA) supplemental test. These tests are currently available in multi-antigen configurations. The EIAs are marketed in the U.S. as either second generation or third generation formats, while the supplemental RIBA test is commercially available in its third generation format.

VI. MARKETING HISTORY

The Home Access® HCV Check℠ is not currently marketed for consumer in-home specimen collection, dried blood spot or other sample, in any country.

VII. ADVERSE EFFECTS OF DEVICE ON HEALTH

There are no known direct adverse effects of this device on the health of the user. However, failure of the test to perform as indicated or human error during performance of the test may lead to a false diagnosis and improper patient management. Additionally, because HCV is highly infectious, incorrect diagnostic information may

lead to the spread of infection from the patient to uninfected members of the community.

During the clinical study, 22 (1.7%) of the 1,286 participants experienced minor adverse events such as dizziness, diaphoresis, and nausea. Ten participants expressed disbelief in the test results. No participant required medical intervention.

VIII. SUMMARY OF STUDIES

Five non-clinical studies and one multicenter clinical trial were conducted to establish the safety and effectiveness of the Home Access® HCV Check℠. A pilot study was conducted to determine if non-medically trained consumers could adequately collect a sufficient dried blood spot (DBS) sample for HCV testing compared to medical professionals.

A. NON-CLINICAL STUDIES

The applicant conducted non-clinical studies to demonstrate the analytical sensitivity, specificity, and reproducibility of the Home Access® HCV Check℠ for use with the proposed DBS method.

1. The analytical sensitivity of the Home Access® HCV Check℠ was compared to matched plasma/serum samples using the blood bank procedure. The data obtained demonstrated that the DBS method used provided analytical sensitivity (detection limit) equal to serum testing using the blood bank procedure.

   Twenty-three commercially obtained anti-HCV seroconversion panels - serial samples - were tested using both methods. The screening results, comparing the DBS elution and EIA testing of the device to the approved serum testing method detected seroconversion at the same draw of blood for 17 panels. The remaining 6 panels differed in seroconversion by only one sample of blood. All repeatedly reactive specimens were tested with the HCV RIBA analysis and the results obtained with DBS and serum were compared. The DBS methodology detected the seroconversion at the same blood sampling time for 20 of 23 panels and the remaining 3 panels differed in seroconversion by one blood sampling time. Six additional samples produced discrepant results: 2 specimens were positive by DBS and indeterminate by serum, and 4 specimens were positive by serum and indeterminate by DBS. 178

2. To further demonstrate the analytical sensitivity of the Home Access® HCV Check℠, the sponsor conducted studies to evaluate its detection of HCV antigenic variability and interference of detection with other disease states. This evaluation was performed using a worldwide HCV performance panel. The panel includes all four of the six recognized serotypes of HCV and their

most common subtypes (1a, 1b, 1a/b, 2a/c, 3a/b, 4c/d, and 4h). These serotypes were isolated from patients in the U.S., Argentina, Egypt, Uganda, and China. All twenty of these samples gave comparable results for the venous samples and the DBS samples. These data demonstrated that the assays could detect all four serotypes from HCV antigenic variability. However there were no data on the other two recognized HCV genotypes. The concordance was 100%.

3. To demonstrate the analytical specificity of the device, specimens from patients with disease states known to interfere with hepatitis antibody assays, (e.g., cytomegalovirus, acute and chronic hepatitis B, hepatitis A, alcoholic cirrhosis, liver cancer, multiple myeloma, and an autoimmune disease) were tested in both anti-HCV positive and negative samples. The specimens were previously characterized, and patient histories and data were provided to show the serological reactivity of those other conditions where appropriate. With one exception, a patient with multiple myeloma, all 69 anti-HCV negative samples produced identical outcomes for DBS testing when compared with matched sera using the blood bank procedure.

   The analytical specificity was also assessed with samples with elevated hematocrits and abnormal triglyceride levels. These data demonstrated no reproducible interference from other viral or immune diseases in anti-HCV positive or negative specimens in either the DBS or serum testing systems. The concordance calculated was 100%.

4. To demonstrate the reproducibility of the test results, the applicant conducted inter-assay and intra-assay precision studies of the Home Access® HCV Check℠ for elution and testing DBS specimens as compared to the HCV EIA tested according to approved manufacturer insert (i.e., venous serum/plasma). The DBS method produced inter-assay and intra-assay standard deviations with negative control values of 0.018 and 0.009 optical density (O.D.) units, respectively. The DBS method produced inter-assay and intra-assay coefficient of variation (C.V.) for the positive control of 3.1 % and 7.8%, respectively. These data are equal to matched sera tested using the blood bank procedure. Lot to lot studies were not conducted. The applicant submitted lot-to-lot release data from the Home Access® HIV kit to show that similar results were obtained using different lots of the blood specimen collection paper. (Note: The Home Access® HIV kit uses the same blood specimen collection paper as the Home Access® HCV Check℠.)

5. Stability studies were conducted to support the claim that the DBS sample is viable up to 10 days under various shipping conditions. The applicant submitted data collected up to 21 days. The data showed stability of the DBS up to 14 days. The stability of the collection device was determined to be 18 months at ambient temperatures.

6. Pilot Study:

The sponsor conducted a preliminary pilot study to determine if non-medically trained consumers could adequately collect a sufficient DBS sample to initiate HCV antibody testing. The consumer test samples were compared to DBS collected by trained professionals. A different elution procedure and analytical method was used in the pilot study. The study provided information on the comparison of the test results of the self-collected DBS samples to the serum samples collected by a medical professional. One participant out of 50 (2%) withdrew from the study following an adverse experience, which consisted of dizziness during self-collection. The adverse experience was minor and no medical intervention was required.

Of the 50 pilot study serum samples tested with the EIA procedure, 45 were HCV antibody nonreactive (negative) and 5 were HCV antibody reactive. Of the 45 venous samples testing EIA nonreactive, 42 DBS tested nonreactive, 1 reactive, and 2 were not tested (insufficient sample). Of the 5 venous samples testing EIA reactive, 4 DBS tested reactive and 1 sample tested nonreactive.

In conclusion, the non-clinical study demonstrated that the Home Access® HCV Check℠ could be used safely and effectively with the proposed DBS specimen. The studies validated the detection limit, analytical sensitivity, analytical specificity, and precision of the Home Access® HCV Check℠. The analytical performance of the DBS specimens was comparable to the standard testing procedure for matched plasma/serum samples. The Pilot study demonstrated that non-medically trained consumers could adequately collect a DBS specimen for HCV testing.

B. CLINICAL STUDIES

A multicenter clinical trial was conducted to demonstrate the safety and effectiveness of the Home Access® HCV Check℠ and to determine the performance characteristics of the device in the intended use population. The objective of the study was to demonstrate that non-medically trained consumers could safely and effectively collect and ship a DBS specimen for HCV testing, retrieve their results by telephone and understand the test results.

The effectiveness of the device was assessed by evaluating the adequacy of self-collected DBS using the Home Access® HCV Check℠ compared with professionally collected DBS. The HCV antibody test results for self-collected DBS were compared to professionally collected venous samples. The participants' comprehension of the pre-test educational session, including categorization of requests to speak with a healthcare counselor, was used to assess the adequacy of the instructions for use of the device. In addition, monitoring adverse experiences related to the self-collection device and the retrieval of test results were used to assess the safety of the device.

There were 1,286 participants enrolled in the study. The consumers were at risk for HCV infection and were untrained in blood collection. The participants used the Home Access® HCV Check℠ in a private room provided by the investigator without the assistance of study site staff. Participants called a toll-free number provided with the service to register their kit, receive educational information, retrieve results, and receive counseling and referrals as appropriate. For study purposes, the test results reported to the participants were their venous sample only, using licensed test reagents and manufacturers' methods. HCV negative results were provided by recorded message unless the participant chose to speak with a Home Access counselor or physician. Non-negative results were provided via a counselor. In addition to HCV healthcare information, counselors provided healthcare referrals as appropriate.

Of the 1,286 participants entered, a total of 1,192 (92.7%) completed all the study procedures and were available for analysis, while 98 participants (7.6%) were considered not to have completed all the study procedures and were excluded from some statistical interpretations. (Excluded were 68 with insufficient blood on the card, 11 with no card in the foil pouch, and 19 with no DBS card.) Overall, 1,246 (96.9%) of 1,286 professionally collected venous samples were adequate for evaluation compared to 1,188 (92.4%) of 1,286 participant self-collected specimens. Compared to adequate venous samples collected by professionals, 95.3% of participants collected adequate DBS specimens. When comparing self-collected DBS to the professionally collected DBS control, 97.0% of participants submitted samples adequate for testing. The absolute percentage of evaluable samples for participants did not differ greatly between participants previously thought to be HCV positive (92.1%) and participants previously thought to be HCV negative (92.8%).

A total of 1,188 (92.4%) of the 1,286 self-collected DBS samples received by the laboratory were suitable to initiate testing. Forty-two participants (3.3%) did not have sufficient blood to complete initial testing (Table 1). The most common reason for unsuitable samples for both DBS and venous collection was insufficient amount of blood collected. (Note: Inconclusive results are not reported to the consumer. The consumer would be notified that he/she did not have sufficient sample to complete testing.)

Table 1
Number of Adequate DBS Samples
Self-Collected vs. Professionally Collected
All Participants (N = 1,286)

	Professional DBS		
Self-Collected DBS	Adequate	Rejected	Total
Adequate	1,143	45	1,188 (92.4%)
Rejected	82	16	98 (7.6%)
Total	1,225 (95.3%)	61 (4.7%)	1,286

Most participants (91.9%) answered the true/false questions regarding HCV correctly after reading the package insert and/or speaking with a Home Access counselor as instructed.

Of the 1,286 participants entered in the study, 22 participants (1.7%) had adverse experiences. Of the 22 adverse experiences, 10 (0.8%) were considered possibly related to the use of the Home Access® HCV Check[sm]. Additionally, 159 (12.4%) participants reported difficulty with specimen collection. The most frequently reported adverse experience was participant disbelief of venous test result (0.8%). There were no serious adverse experiences.

The population tested included 345 persons known to be HCV positive, 327 persons at high risk for HCV infection (receiving blood or blood products or organ transplants before 1990), 119 persons on hemodialysis, 403 non-prescription IV drug users, 159 persons who had sexual contacts with HCV infected persons, and 401persons who had an HCV positive household member, 5 healthcare workers exposed to blood or blood products, and some low risk individuals. The genotypes of the HCV that infected these individuals were not identified.

Of the 1286 DBS samples collected, 98 (7.6%) were not tested. When the DBS EIA test results were compared to the venous EIA results, the following results (Table 2) were obtained:

Table 2

		EIA Venous Results		
		Negative	Reactive	Inconclusive
Self-Collected DBS EIA Results	Negative	677	9	0
	Reactive	10	416	1
	Inconclusive	2	37	0

There were 10 (0.8%) False Negative and 9 (0.7%) False Positive EIA results, and 39 samples with inconclusive results.

When the DBS self-collected sample results were assayed with the RIBA assay and compared to the venous RIBA results the following data (Table 3) was obtained:

Table 3

		RIBA Venous Results			
		Negative	Reactive	Indeterminate	Inconclusive
Self-Collected DBS RIBA Results	Negative	7	2	6	0
	Reactive	0	344	3	0
	Indeterminate	4	2	6	0
	Inconclusive	2	94	2	10

If the indeterminate and inconclusive results were excluded, using DBS samples, the RIBA assay sensitivity was 98.2% and specificity was 99.6%.

When the data was stratified by risk, the following data (Tables 4, 5) were observed:

Table 4

EIA Results	Reactive	Non-Reactive	Not Tested (QNS)	Inconclusive
Low Risk	15	267	3	5
High Risk	154	414	46	15
Previous HCV+	282	14	25	24
Totals	451	695	74	44

Table 5

RIBA Results	Reactive	Negative	Indeterminate	Inconclusive	Not Tested
Low Risk	8	2	3	5	27
High Risk	110	4	6	49	46
Previous HCV+	246	2	3	55	25
Totals	364	8	12	109	98

In summary, the Home Access® HCV Check℠, in a setting that closely approximates its intended use population, demonstrated the ability of non-medically trained users to self-collect specimens suitable for testing. When compared with professional DBS collection, participants successfully collected suitable DBS specimens 97.0% of the time and DBS yielded results similar to venous collection.

IX. CONCLUSIONS DRAWN FROM THE STUDIES

A. Conclusions Drawn from Non-clinical Studies:

In blinded non-clinical evaluations of the performance of the elution and testing method, the analytical sensitivity (detection limit) of the Home Access® HCV Check℠ was shown to be equivalent to or better than serum testing venous samples using the Blood Bank Algorithm. These studies, evaluating performance

in seroconversion panels, dilutions of known positive specimens, world-wide performance panels, and interfering disease states demonstrated:

1. Detection of Seroconversion - Of 23 commercial anti-HCV seroconversion panels, the DBS elution and EIA testing methods of the proposed device detected seroconversion at the same time for 17 panels compared to the approved serum testing method.

2. Detection of Serial Dilution of HCV Positive Specimens - The DBS and serum EIA results for testing of serial dilutions were concordant for all but two samples which remained reactive at 1:1000 dilution using DBS testing but were non-reactive on serum testing.

3. Detection of HCV Subtypes and Variants - Of the world-wide performance panel of 86 serum/plasma specimens known positive specimens, all were properly characterized as anti-HCV positive with the proposed device.

4. Lack of Interference of Concomitant Disease States - Interfering substances produced the same result for 68 of 69 specimens (one known positive tested indeterminate in supplemental testing) of anti-HCV positive or negative sera spotted onto dried blood spots. Identical outcomes for the two methods demonstrated no reproducible interference of other common diseases with either HCV positive or negative specimens in either the DBS or serum testing systems.

5. Comparison of Proposed Method to Serum Testing. These results validated the analytical sensitivity (detection limit) observed in the prospective clinical trial conducted on the Home Access Hepatitis C Test Service for DBS compared to the standard testing procedure for matched plasma/serum samples commonly referred to as the blood bank algorithm.

B. Conclusions Drawn From Clinical Studies

In prospective multi-center clinical evaluations of the performance of the Home Access® HCV Check℠ home specimen self-collection, testing and counseling product yielded test results very similar to testing venous blood drawn by a medical professional. This study demonstrated:

1. Safety of the proposed device - There were 22 (1.7%) adverse experiences reported among the 1,286 participants. Of these, 10 (0.8%) were determined by investigators as having some relationship to the investigational device and 12 were determined not related to the device in any way. The minor events included dizziness upon sticking the finger or disbelief of a positive HCV test result. These were not considered serious adverse events. Medical intervention was not required for any of the events.

2. Ability to Collect an Adequate Sample - Sample adequacy evaluation demonstrated that 1,188 (92.4%) of the 1,286 self-collected DBS samples received by the laboratory were suitable to initiate testing. As a result of having sufficient blood to complete initial testing only, 42 participants (3.3%) would have received inconclusive results. Compared with medical professional DBS collection, participants adequately obtained suitable samples 97.0% of the time.

3. Performance of Dried Blood Spot Specimens Compared to Serum Testing - The performance of self-collected DBS specimens correlated satisfactorily to testing professionally collected serum specimens with a concordance of 99.8%.

C. Risk – Benefit Analysis

The clinical studies contained in this submission demonstrated that non-medically trained individuals could safely and effectively collect a DBS specimen and ship it to a central laboratory for analysis. Both the nonclinical and clinical studies provided evidence that the DBS elution and analysis testing using licensed reagents produced test results with sensitivity and specificity that is comparable to serum or plasma testing. Consumers using this service were able to retrieve their results, receive educational risk information, counseling, and healthcare referrals if requested, in a safe and effective manner.

In the prospective clinical studies reported, the Home Access ®HCV Check[sm] was safe and produced minimal minor adverse health consequences.

It can therefore be concluded that the benefits of the Home Access® HCV Check[sm] outweigh the possible risks associated with its use.

X. PANEL RECOMMENDATION

Pursuant to section 515 (c) (2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not the subject of an FDA Microbiology Devices advisory Panel meeting because the information in the PMA substantially duplicates information previously reviewed by this panel.

XI. CDRH ACTION ON THE APPLICATION

CDRH issued an approval order for the applicant's PMA for the Home Access® Hepatitis C Check[sm] and Hepatitis C Check[sm] Express on April 28, 1999.

The applicant's manufacturing and control facilities were inspected on March 26, 1999 and the facilities were found to be in compliance with the Good Manufacturing Practice Regulations (GMPs). The shelf-life of the Home Access® HCV Check[sm] has

been established at 18 months when stored at 26 to 35 degrees centigrade. (Note: After the approval order was issued the applicant submitted an annual report that contained additional stability data to extend the shelf-life to 25 months.)

XII APPROVAL SPECIFICATIONS

Directions for use: See labeling

Conditions of Approval: CDRH approval of this PMA is subject to full compliance with the conditions described in the approval order.

XIII. REFERENCES

1. Parker SP, Cubitt WD, Ades AE. A Method for the Detection and Confirmation of Antibodies to Hepatitis C Virus in Dried Blood Spots. J. Virol. Meth. 1997; 68:199-205.

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